IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellants(s):	Shaun A. Kirkpatrick, et al.	**Examiner:**	Konstantina Katcheves
Serial No.:	09/433,429	**Art Unit:**	1636 #20
Filed:	November 4, 1999	**Docket:**	11160
For:	PRODUCTION OF A BIOLOGICAL FACTOR AND CREATION OF AN IMMUNOLOGICALLY PRIVILEGED ENVIRONMENT USING GENETICALLY ALTERED SERTOLI CELLS	**Dated:**	May 9, 2003

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' BRIEF ON APPEAL

I. INTRODUCTION

Appellants, through the undersigned, hereby submit this Brief on Appeal pursuant to 37 C.F.R. §1.192 in response to the decision of the Examiner, mailed June 3, 2002, finally rejecting claims 18-20 and 25-31.

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents and Trademarks, P.O. Box 1450, Alexandria, VA 22313-1450 on May 9, 2003

Dated: May 9, 2003

Michelle Mustafa

II. REAL PARTY IN INTEREST

The real party in interest in the above-identified appeal who has been assigned the entire right, title and interest in the above-identified application is Sertoli Technologies, Inc., 101 North Wilmot Road, Suite 600, Tucson, AZ 85711-3335.

III. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

IV. STATUS OF CLAIMS

The present application was filed on November 4, 1999 claiming the benefit of U.S. Provisional Application Serial No. 60/107,438, filed on November 6, 1998.

The present application was filed with 26 claims. Following a Restriction Requirement dated January 2, 2001, Appellants elected to prosecute claims 18-26 on February 22, 2001. Claims 21-24 were cancelled without prejudice, claims 18-20 and 25-26 were amended and new claims 27-31 added by amendment dated January 8, 2002. Therefore, the pending claims are 18-20 and 25-31. These claims, which are the subject of this appeal, are set forth in the Appendix of this Appeal Brief, and attached hereto. Each of these claims has been finally rejected and are on appeal.

V. STATUS OF AMENDMENTS

Claims 18, 19, 20 and 27-28 were cancelled without prejudice after issuance of the Final Rejection by amendment dated December 3, 2002. The after-final amendment was not entered into the record according to an Advisory Action dated January 6, 2003, which alleged that the "proposed amendment(s)...are not deemed to place the application in better form for appeal by materially or simplifying the issues for appeal".

VI. SUMMARY OF THE INVENTION

The Claims on appeal relate to Sertoli cells comprising a vector having a promoter operatively linked to a coding sequence for a biological factor wherein the Sertoli cell creates a immunologically privileged site *in vivo* and vectors which function in Sertoli cells comprising promoters operatively linked to a coding sequence for a biological factor; e.g. B-UGT, insulin, IL-2, dopamine or GM-CSF.

The present invention is directed to Sertoli cells which comprise a biological factor wherein the Sertoli cell creates an immunolgically privileged site *in vivo* and vectors which function in Sertoli cells operatively linked to a coding sequence for a biological factor that have not been realized heretofore. For example, the invention contemplates a vector linked to a DNA or RNA sequence coding for a particular protein which is placed within a vector which can replicate within a Sertoli cell, the Sertoli cell can create an immunologically privileged environment *in vivo* thereby permitting the expression of a protein in the Sertoli cell, without stimulating an autoimmune response.

The claims define various embodiments of the present invention. In one embodiment, recited in claim 25, the present invention is directed to a Sertoli cell comprising:

a vector comprising, in the 5' to 3' direction, a promoter which functions in Sertoli cells, operatively linked to a coding sequence for a biological factor wherein said Sertoli cell creates an immunologically privileged site *in vivo*.

Support for the claimed Sertoli cells is found on page 14, line 27-page 15, line 12 of the instant specification. Examples of the Sertoli cells comprising the expression vectors

employed in accordance with the claimed invention is found at Example 5, pages 43-44. Reference is also made to the discussion hereinbelow under ARGUMENTS FOR PATENTABILITY.

VII. ISSUES ON APPEAL

Is the subject matter in claims 18-20 and 25-31, directed to Sertoli cells and vectors functional in Sertoli cells, rendered obvious by a combination of Gorman, European Patent Application No. 0 260 148 (hereinafter "Gorman") in view of Builder et al., U.S. Patent No. 5,663,304 (hereinafter "Builder et al."), Meulien, U.S. Patent No. 5,521,070 (hereinafter "Meulien"), Ritter et al., (1991) J. Biol. Chem. 266:1043-1047 (hereinafter "Ritter et al.") and Ciotti et al. (1996) Biochem. 35:10119-10124 (hereinafter "Ciotti et al.") when there is no suggestion or motivation therein of a vector or a Sertoli cell comprising a vector which functions in the Sertoli cell, operatively linked to a coding sequence for a biological factor wherein the Sertoli cell creates an immunologically privileged site *in vivo*, which would be achieved with a reasonable expectation of success.

VIII. GROUPING OF THE CLAIMS

The involved claims stand or fall together.

IX. ARGUMENTS FOR PATENTABILITY

THE REFERENCES CITED BY THE EXAMINER DO NOT TEACH, DISCLOSURE OR SUGGEST THE CLAIMED INVENTION

Appellants submit that none of the cited references teach or disclose a vector comprising a coding sequence for a biological factor wherein said sequence codes for human factor IX, bilirubin UDP-glucuronosyltransferase, insulin, IL-2, dopamine, GM-CSF, M-CSF or TNF, as presently claimed. Moreover, none of the cited references teach a Sertoli cell

comprising the vector which functions in a Sertoli cell operatively linked to a coding sequence for a biological factor wherein the Sertoli cell creates an immunologically privileged site *in vivo*.

The Examiner alleges that Builder et al. teach expression of DNA encoding a desired polypeptide and a suitable host cell appropriate for the expression of the DNA encoding the desired polypeptide. The Examiner also alleges that useful mammalian host cells such as mouse Sertoli cells are contemplated by Builder, et al.

The Examiner further alleges that expression of desired polypeptides include Factor VIIIC and Factor IX. The Examiner concedes that Builder, et al. do not provide working examples of Sertoli cells comprising vectors encoding factor VIII or factor IX and that Builder, et al. do not specifically mention bilirubin UDP-glucuronosyltransferase.

The Examiner alleges that Muelien, et al. teach that in the sequence coding for Factor IX there is a signal sequence encoded in the cDNA. The Examiner admits that Muelien, et al. do not teach Sertoli cells. Similarly, although Ritter, et al. are alleged to teach the cloning of cDNAs for two bilirubin UDP-glucuronosyltransferases, Ritter, et al. do not teach Sertoli cells. Finally, the Examiner alleges that Ciotti, et al. teach vectors comprising bilirubin UDP-glucuronosyltransferase, but like Muelien, et al., and Ritter, et al., Ciotti, et al. do not teach Sertoli cells. Nevertheless, the Examiner alleges that at the time of the invention, the skilled artisan would have been motivated to express in cells "any biological factor (polypeptide) of interest, especially polypeptides of importance to human biology, such as factor VIII, factor IX or bilirubin UDP-glucuronosyltransferase... so that the polypeptide could be produced and either used for therapeutic purposes or studied in vitro...".

Appellants respectfully submit that the prior art does not provide any suggestion or motivation to make the claimed invention. There is no motivation, teaching or suggestion in

the cited references to combine the teachings of Gorman, Builder, et al., Muelein, Ritter, et al. and Ciotti, et al. Such combination does not arrive at the presently claimed invention in any event.

The Examiner alleges that the skilled artisan would have been aware of "teachings of expression of polypeptides in different types of cells, as such references would all be analogous art and different cells that were shown to be successful for expression of biological factors would be art-recognized equivalents of one another". No references are provided in support of this blanket assertion. Moreover, the Examiner alleges that one would have been motivated to use a promoter that functioned in the cells so that the desired polypeptides would be expressed.

Builder, et al. teach expression of DNA encoding a desired polypeptide. Builder, et al. provide no suggestion, motivation or teaching no less any recognition of a Sertoli cell which creates an immunologically privileged site for the biological factor expressed thereby. The secondary references, Muelein, et al., Ritter, et al., and Ciotti, et al., do not even teach Sertoli cells. Appellants submit that the Examiner has taken bits and pieces of Builder, et al., Muelein, et al., Ritter, et al., Ciotti, et al. and Gorman and interpreted such disclosures in a way that was not intended and is not correct. Moreover, the secondary references fail to ameliorate the deficiencies of Builder, et al. and Gorman. Appellants therefore submit that the interpretation urged by the Examiner is too broad given the clear teaching of the references, the Examiner's own admissions and the state of the claims.

The rejection of claimed subject matter as obvious under 35 U.S.C. §103(a) in view of the combination of prior art references requires that the suggestion to carry out the claimed invention must be found in the prior art, not in Appellants' disclosure. In re Vaeck, 947

F2d 488, 493, 20 U.S.P.Q. 2d 1438, 1442 (Fed. Cir. 1991). In In re Vaeck, the Appellants claimed a Bacillus gene in a host cyanobacteria that produced an insecticidal protein. The prior art taught both the gene and the bacterium, but did not teach the combination as described by Appellants. The court held the claimed invention was not obvious stating:

> The prior art in this case offers no suggestion, explicit or implicit, of the substitution that is the difference between the claimed invention and the prior art. In re Vaeck, 947, F2d 495, 20 USPQ 2nd at 1444.

In the present case the Examiner has not met the burden of demonstrating either an explicit or implicit suggestion in the prior art to combine the teachings of Builder, et al., Gorman, Muelein, Ritter, et al. and Ciotti, et al. in order to achieve the claimed invention. There must be an indication in the prior art as a whole to suggest the desirability, and thus the obviousness of making the combination. In re Newell, 891 F2d 899, 901, 13 USPQ 2d 1248, 1250 (Fed. Cir. 1989). There is no such suggestion identified on this record.

Assuming, pro arguendo, the generalized teachings of Sertoli cells and vectors in the cited references, Appellants submit that there is simply no suggestion or motivation to construct a Sertoli cell which comprises a vector comprising a promoter operably linked to a coding sequence for a biological factor, wherein the Sertoli cell creates an immunologically privileged site *in vivo*. The genetically altered Sertoli cells of the present invention provide an immunologically privileged site *in vivo* as measured, for example, by functional assessment of the biological factor produced by the cells. The cited references fail to appreciate, no less motivate the skilled artisan to create altered Sertoli cells, as claimed. Support for the *in vivo* immunoprivileged environment is found throughout the specification and particularly at page 6, lines 14-17, for example; in full satisfaction of the requirements of 35 U.S.C. §112, first paragraph.

X. CONCLUSION

The above arguments clearly overcome the rejections in the Final Action and clearly establish that all of the claims on appeal are patentable. Affirmance of the patentability and reversal of the Final Rejection of the claims on appeal are respectfully solicited.

Respectfully submitted,

Peter I. Bernstein
Registration No. 43,497

Scully, Scott, Murphy & Presser
400 Garden City Plaza
Garden City, New York 11530
(516) 742-4343

PIB:dg

APPENDIX

18. A vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for human factor IX.

19. The vector of Claim 18 further comprising a 3' termination sequence which function is Sertoli cells.

20. The vector of Claim 18 or 19 further comprising a signal sequence coding for a signal peptide, said signal sequence located downstream from said promoter.

25. A Sertoli cell comprising a vector comprising, in the 5' to 3' direction, a promoter which functions in Sertoli cells, operatively linked to a coding sequence for a biological factor wherein said Sertoli cell creates an immunologically privileged site *in vivo*.

26. A Sertoli cell comprising a vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor and a signal sequence coding for a signal peptide, said signal sequence located downstream from said promoter, wherein said Sertoli cell creates an immunologically privileged site *in vivo*.

27. A vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for bilirubin UDP-glucuronosyltransferase (B-UGT).

28. A vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for any one of the following groups consisting of insulin, IL-2, dopamine, GM-CSF, M-CSF or TNF.

29. A Sertoli cell comprising a vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for factor VIII and wherein said Sertoli cell creates an immunologically privileged site *in vivo*.

30. A Sertoli cell comprising a vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for factor IX and wherein said Sertoli cell creates an immunologically privileged site *in vivo*.

31. A Sertoli cell comprising a vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for bilirubin UDP-glucuronosyltransferase (B-UGT) and wherein said Sertoli cell creates an immunologically privileged site *in vivo*.